Studies on Enzyme Action. XXIII.—*Homo- and Hetero-lytic Enzymes.*

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From the evidence given by Prof. Hopkins and his co-workers, it is clear that the agent in milk which induces the oxidation of both xanthin and hypoxanthin, in presence of either methylene blue or oxygen, is a *catalyst,* in the sense defined by my son and myself* and justified by his later observations on the hydrogenation of oils in presence of nickel: as the change proceeds at the linear rates characteristic of catalytic action, when unhampered by secondary effects. Moreover, the catalyst is so selective in its action, that we are justified in regarding it as an enzyme: an enzyme being a colloid, selective catalyst.

The most remarkable result of the inquiry is the establishment of the fact, that the two bases are "hydroxylated" at molecularly equal rates, although twice the work is done upon the one as upon the other. The following may be put forward as perhaps not too daring an explanation of this novel observation.

With reference to the equivalence of methylene blue and oxygen, oxidation, it is to be noted, is a process in which the oxygen used plays only a secondary part, as it were—that of the depolariser; the active hydroxylating agent is the hydroxyl of hydrone, *i.e.*, the fundamental molecule of water, the change being effected in an electrolytic circuit, thus—

$$\begin{array}{c|ccc|cc|c|cc}
\mathrm{O} & \mathrm{H} & \ldots\ldots & \mathrm{OH} & & \mathrm{OH} & \ldots\ldots & \mathrm{OH} & \\
| & & & & X = & | & & & X. \\
\mathrm{O} & \mathrm{H} & \ldots\ldots & \mathrm{OH} & & \mathrm{OH} & \ldots\ldots & \mathrm{OH} &
\end{array}$$

X is the oxidised material. Methylene blue may be set in the place of oxygen, in this expression. Presumably, the only difference in their action is that the primary product from oxygen, perhydrone (hydrogen peroxide), can act again in like manner, so that oxygen has double the value of methylene blue. We have to dissociate from our minds the ordinary idea that oxygen is itself an oxidising agent acting directly.

The authors were unable to obtain the effect with hydrogen peroxide; maybe the concentration was too great or the enzyme may have been affected and, if not destroyed, thrown out of action. The behaviour of enzymes towards perhydrone is known to be peculiar.

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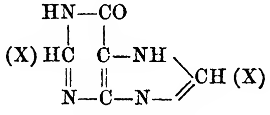
* 'Roy. Soc. Proc.,' B, vol. 86, p. 561 (1913).

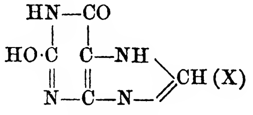
As to the enzyme, it appears that this can influence or direct attack, *at two centres simultaneously* in hypoxanthin, whilst it affects *only one* in xanthin; it is, therefore, probable that the enzyme *fits* a large section, if not the whole of the molecule.

An enzyme which could thus act may be imagined, containing as active component uric acid itself; this might be compatible with both molecules, as the CH group to be oxidised would probably be no obstacle to its fit, whilst the presence of NH in place of O in the allied bases, adenine and guanine, would certainly be an interference. It is possible to think of such an enzyme becoming "perhydroxylised" under the influence of the hydrogen acceptor and of the product as inducing, in turn, the hydroxylation of one or both sensitive centres in the two bases. The effect on hypoxanthin would be like that of using two voltaic cells in series, instead of a single cell of about half their joint electromotive force.

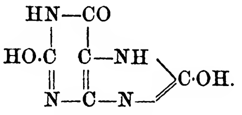
The striking similarity in the two bases and uric acid is brought out clearly, when the lower two-thirds of their formulæ are compared, X being the centre at which hydroxylation takes place:—



Hypoxanthin.



Xanthin.



Uric acid.

The effect of the milk enzyme—Xanth-hydroxylase (?)—is essentially hydrolytic: differing only from that of enzymes ordinarily classed as hydrolytic in that, instead of inducing the distribution of the elements of the hydrone molecule between the two sections of a single molecule of the hydrolyte, it is the cause of the inclusion of two distinct molecules in the circuit of change. This latter mode of action is clearly operative in the later stages of alcoholic fermentation. I would suggest that the two classes of enzyme be distinguished as *homo-* and *hetero-lytic.*

Our knowledge of the nature of the oxidases and peroxydases has hitherto been vague; the proof now afforded that a member of the class is an enzymic catalyst is most welcome, the more as so remarkable a double behaviour has been brought to light.